## **Claims**

- 1. A library of nucleic acid molecules, each molecule comprising an open reading frame and lacking the 3'-untranslated region normally associated with said open reading frame.
- 5 2. The library of claim 1, wherein said nucleic acid is RNA.
  - 3. The library of claim 2, wherein said RNA is messenger RNA.
  - 4. The library of claim 2, wherein said RNA is cellular RNA.
  - 5. The library of claim 4, wherein said cellular RNA is derived from a eukaryotic organism.
  - 6. The library of claim 5, wherein said cellular RNA is derived from a mammal.
    - 7. The library of claim 6, wherein said mammal is a human.
    - 8. The library of claim 1, wherein said nucleic acid is DNA.
- 9. The library of claim 1, wherein said library comprises at least 10<sup>5</sup> members.
  - 10. The library of claim 1, wherein said nucleic acid molecules of said

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library also lack stop codons.

- 11. A library of nucleic acid molecules produced by the steps of:
- (a) providing a library of DNA molecules, each having an open reading frame and a 3'-untranslated region, each of said DNA molecules terminating at its 5' end in an overhang and at its 3' end in a blunt end; and
- (b) treating said library of DNA molecules first with a 3'→5' exonuclease and then with a single-stranded nuclease under conditions that allow removal of the 3'-untranslated regions of said DNA molecules.
  - 12. A library of nucleic acid molecules produced by the steps of:
- (a) translating a library of mRNA molecules *in vitro* in a translation reaction mixture lacking functional translation release factor activity, resulting in pausing of the translation reaction mixture ribosomes at the stop codons of said mRNA molecules;
- (b) adding, to said translation reaction mixture of step (a), reverse transcriptase and oligonucleotide primers which are complementary to the 3'-untranslated regions of said mRNA molecules at a site proximal to said stop codons, under conditions which allow the synthesis of strands of DNA that are complementary to said 3'-untranslated regions and terminate at sites proximal to said stop codons; and
- (c) removing the RNA portions of the RNA-DNA duplexes formed in step (b), thereby removing the 3'-untranslated regions of said mRNA molecules.
  - 13. The library of claim 12, produced by the further steps of:

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- (d) ligating to each of the 3' ends of the products of step (c) a linker comprising a Type IIS restriction site;
- (e) extending the products of step (d) to produce double-stranded DNA molecules; and
- f) treating said double-stranded DNA molecules with a Type IIS restriction enzyme that recognizes said Type II restriction site to cleave said DNA molecules and remove said stop codons.
  - 14. A library of nucleic acid molecules produced by the steps of:
  - (a) providing a population of mRNA molecules;
  - (b) synthesizing strands of DNA, each of which is complementary to one of said mRNA molecules, using a random primer mixture, said random primer mixture comprising primers, each having
  - (i) a 3' region comprising a stop codon flanked by a random oligonucleotide located 3', 5', or both to said stop codon; and
    - (ii) a 5' region comprising a Type IIS restriction site;
  - (c) ligating to the 3' ends of the DNA products of step (b) an oligonucleotide tail;
    - (d) amplifying the products of step (c) using
  - (i) a first primer which is complementary to said Type IIS restriction site-containing sequence; and
  - (ii) a second primer which is complementary to said oligonucleotide tail; and
  - (e) treating the products of step (d) with a Type IIS restriction enzyme that recognizes said Type IIS restriction site to cleave said products, thereby removing the 3'-untranslated regions and stop codons.

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- 15. The library of nucleic acid molecules of claim 14, produced by the further steps of:
- (f) ligating a sequence which encodes an affinity tag to the cleaved ends of the products of step (e);
  - (g) transcribing the products of step (f);
- (h) ligating peptidyl acceptors to the 3' ends of the RNA products of step (g);
- (i) translating said products of step (h) to produce a population of RNA-protein fusions; and
- (j) substantially isolating RNA-protein fusions which comprise said affinity tag, thereby obtaining a population of mRNA molecules lacking 3'-untranslated regions and stop codons.
  - 16. A library of nucleic acid molecules produced by the steps of:
  - (a) providing a population of mRNA molecules;
- (b) synthesizing strands of DNA, each of which is complementary to one of said mRNA molecules, using a random primer mixture, said random primer mixture comprising primers, each having (i) a 5' region which lacks a stop codon in at least one reading frame and (ii) a random 3' region; and
- (c) synthesizing strands of DNA complementary to said DNA strands of step (b), using a second random primer mixture.